



Do we need a national antiretroviral treatment register?

Combination antiretroviral therapy (ART) has greatly improved the prognosis of HIV-infected individuals in affluent countries, resulting in a marked drop in AIDS-related mortality.¹⁻³ ART programmes have also been successfully initiated in less well-resourced health systems. Brazil, a middle-income developing country, has incorporated ART into its public health service⁴ and a successful ART programme has been implemented in rural Haiti, the poorest country in the Western hemisphere.⁵

Results from a South African community clinic-based ART programme were reported on by Bekker *et al.* in the June issue of the *Journal*.⁶ Despite the costs of ART, the beneficial impact on morbidity and mortality has resulted in the World Health Organisation calling for expanded access to ART in resource-poor countries.⁷ While access to ART in South Africa has until recently been limited largely to the private sector,⁸ elements of civil society are now demanding increased access to ART in the public health sector.⁹ Recently a costing model of a limited national ART programme was shown to be affordable¹⁰ and prospects for ART in the South African public sector may have been further increased with the provisional allocation of R1.9 billion for ART in the 2003 national budget. With 350 000 AIDS cases in South Africa¹¹ the scale of an ART programme will need to be of a similar magnitude to that of the TB treatment programme. Concerns have, however, been raised that 'Widespread, unregulated access to antiretroviral drugs in sub-Saharan Africa could lead to a rapid emergence of resistant viral strains, spelling doom for the individual, curtailing future treatment options and leading to transmission of resistant virus'.¹² This pessimistic scenario is far from inevitable if a well-organised national treatment plan is developed. A successful ART programme will face similar challenges to those of the TB control programme, where high levels of adherence are required to a prolonged course of potentially toxic drugs. The TB control programme utilises a standard two-scheduled approach to drug therapy, which simplifies the operational implementation necessary for a large national programme. The national TB register allows performance assessments to be made of individual clinics and the programme as a whole. Similarly a scheduled ART approach would simplify training and education of medical personnel and would result in predictable patterns of toxicity and resistance. A predetermined standardised sequence of drug combinations would also limit the number of drugs to be procured and managed.

The major outcomes of a successful ART programme would be a decrease in AIDS morbidity and mortality. While CD4 cell counts, clinical stage and viral load determine prognosis of untreated patients, effective viral suppression by ART is the major determinant of outcome on treatment.¹³ National and

international ART guidelines have been developed and published which give clear initiation criteria and recommended therapy combinations, which could be used as a basis for scheduled drug choice.^{7,14} A simple register documenting entry criteria and recording scheduled ART therapy would allow an overall audit of programme performance in a similar fashion to that of the TB register. Incorporation of the patient's national ID number in conjunction with national death registration data would allow for calculation of the survival of patients entering the programme on an 'intention to treat' basis. Comparison of these data with modelled survival of patients determined by baseline characteristics on entry to the programme would allow for calculation of life-years gained by the programme. A national ART programme would utilise large quantities of relatively expensive drugs and the financial burden of poor drug accountability could seriously undermine such a programme. The ART treatment register at any institution could be reconciled against drug purchases by that institution for drug accountability purposes and to identify and avoid 'drug seepage'. Specific questions such as impact of prior mother-to-child transmission (MTCT) exposure on response to ART could be answered by analysis of the register database. Blood sampling at the time of failure of the first schedule could also be stored for national viral genotyping surveys, which could give information on viral resistance patterns, which in turn would allow scientific-based changes in scheduled drug choices.

An ART register would need to be a standardised form that could be in either paper- or web-based formats. As ART will be provided at health care facilities other than TB clinics the administration of the register would need to be the responsibility of organisations such as national or provincial AIDS directorates.

To avoid ART anarchy, it has been suggested that the ART programme be closely linked and managed within the TB control programmes of sub-Saharan Africa.¹² ART cannot, however, be isolated from the wider comprehensive approach to HIV and AIDS patient care, including management of the psychosocial and other medical complications such as prophylaxis and treatment of opportunistic infection.^{7,9} It would be neither practical nor prudent to burden the TB control programme with this heavy responsibility. A scheduled ART approach could be a useful method to enable wider, more equitable access to ART within our existing health infrastructure and an ART register would be a tool to monitor the overall performance of such an expanded access programme and allow comparison between sites and delivery models. While expanded access to ART should not be the responsibility of the TB clinics there may be important lessons



to be learned from the programmatic methodological approaches of the national TB control programme.

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Excessive weight gain following therapy for hyperthyroidism — a major problem

One of the most characteristic presenting features of hyperthyroidism is weight loss, despite an increased appetite. This phenomenon is easily understandable, as hyperthyroidism is accompanied by a rise in metabolic rate, energy expenditure and thermogenesis which is clearly not matched by an increased appetite and caloric intake in the vast majority of patients. Consequently a decrease in adipose tissue and muscle results. (Curiously a small proportion of hyperthyroid patients, fewer than 10%, present with weight gain owing to an increased appetite that exceeds the rise in metabolic rate.¹)

Intuitively, one might assume that restoration of thyroid hormone levels to normal would result in the return of weight to premorbid levels. Unfortunately, the insidious presentation of hyperthyroidism, and inaccurate recall by patients, complicate a true assessment of premorbid weight. Nevertheless, just over half of the respondents to a questionnaire sent to women treated for hyperthyroidism reported experiencing a weight problem over a mean follow-up period of 4 years.² Furthermore, numerous reports, including that by Brunova *et al.*³ in this issue of *SAMJ* (p. 529), corroborate the notion that weight gain following therapy for hyperthyroidism is frequently excessive. A mean increase in weight of between 1.55 and 16.4 kg has been reported following anti-thyroid therapy.^{2,6} Indeed, patients attending our clinic have become aware of this phenomenon, as they commonly express concern that treating their hyperthyroidism will lead to excessive weight gain.

Brunova *et al.* report a retrospective analysis of 160 patients

who were treated for hyperthyroidism; 147 were treated with radioactive iodine, 3 underwent thyroidectomy and the remainder received carbimazole. Hypothyroidism ensued in 86.7% of the former two groups and was treated with thyroxine.³ As the premorbid weight could not be ascertained accurately, the baseline weight was taken as the weight at presentation. Weight gain was noted for 24 months, but it stabilised thereafter. The median weight gain found was 5 kg, 6 months after definitive therapy, 9 kg after 12 months and 12 kg after 24 months. Importantly, 29% of their cohort were overweight at presentation (body mass index (BMI) > 25 kg/m²) and 19.3% were obese (BMI > 30 kg/m²). Two years after treatment, 51.3% had become obese, representing a 32% increase in the prevalence of obesity.

Notable predictors of weight gain in studies of patients treated for hyperthyroidism have included a history of weight loss prior to diagnosis, pre-existing obesity, a diagnosis of Graves' disease and the development of hypothyroidism, even transiently.⁵ In contrast, patient age, sex and mode of therapy have not been predictive.^{2,5} Brunova *et al.* described similar major factors associated with increased weight gain, i.e. the diagnosis of Graves' disease, need for thyroxine therapy and poor control of thyroid function on such replacement therapy.³ Yet the extent of weight gain and the rise in the prevalence of obesity was greater than reported by others. For example, Dale and colleagues, who also did not know patients' premorbid weight, described a mean weight gain of 5.4 ± 0.5 kg and an 18.5% prevalence of obesity.⁵ Possible explanations for these